UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,442	06/11/2001	Vincent Dubois	MXI-321CP	3549

959 7590 04/05/2006

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/879,442	DUBOIS ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-21,23-30,37 and 118-124* is/are pending in the application.

4a) Of the above claim(s) *9,10,12,20,21 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-8,11,13-19,23-26,28-30,37 and 118-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claims 2, 3, 5-21, 23-30, 37 and 118-124 are pending in the response filed January 3, 2006.

Response to Amendments / Arguments

Applicant's arguments and amendments filed January 3, 2006 have been considered.

Any rejection not specifically addressed is herein withdrawn.

Allowable Subject Matter

The indication of allowable subject matter, specifically that recited in claims 28, 119 and 120, is withdrawn for the reasons set forth below under 35 USC § 103 and Double Patenting.

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, 120 and 122-124 are readable upon Applicant's initially elected species Suc-βAla-Leu-Ala-Leu-Dox (*see Remarks*, 8/26/04).

Claims 9, 10, 12, 20, 21 and 27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 26, 2004.

Please note, in the interest of compact prosecution and for Applicant's benefit, claims 9, 10, 20, 21 and 27 have been considered insofar as Double Patenting issues only, and does not imply that the claims have been examined under any other statute.

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, and 120-124 have been examined on the merits.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, Table 4, page 53 recites two sequences which require SEQ ID NOs which

are not found in the sequence listing filed.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual – ePave)

2. US Postal Service:
Commissioner for Patents
PO Box 22313-1450
Alexandria, VA 22313-1450

3. Hand carry, Federal Express, United Parcel Service, or other delivery service:
U.S. Patent and Trademark Office
Mail Stop Sequence
Customer Window, Randolph Building
401 Dulany Street
Alexandria, VA 22314

Specification

The specification is objected to because two sequences are recited for which no SEQ ID

NO is found, specifically at page 53, Table 4. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19 and 121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites various acids which would not have a 'negative charge' when coupled to the N-terminus of the peptide, and thus there is insufficient antecedent basis for this limitation in the claim. Specifically, pyroglutamic acid, acetic acid, gluconic, 1- and 2- naphthylcarboxylic acids, polyethylene glycolic acid, and caboxyphenyl boronic acid would not have a negative charge, as the amide bond forms between the lone carboxylate and the amine. Butane disulfonic acid and the remainder of the compounds do not *per se* have a negative charge, except under specific conditions which favor deprotonation of the free carboxylate (or sulfonate), and thus do not have a 'negative charge'.

Claim 121 recites, "of claim 1". Claim 1 is cancelled, and thus does not provide support for antecedent basis in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 3, 4-8, 11, 13-17, 19, 25, 26, 30 and 118 are rejected/remain rejected as being unpatentable under 35 USC § 103(a) for the reasons of record and the following reason. Applicant asserts that the claim amendments overcome the rejection, however, instant claim 19 recites that polyethylene glycolic acid (PEG-acid) is a stabilizing group which maintains dependency from claim 5, and thus PEGylation must still be readable upon the claims, as PEG-acid is a reactant used to make the PEGylated proteins.

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, 120 and 122-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over TROUET (WO 96/05863 A1; F14: PTO-1449 of 11/30/01 – considered with English equivalent provided by Applicant 11/4/04, *see Page 4 Office Action mailed 11/4/04*) in view of LI (PTO-892, 11/4/04) or DeJongh (PTO-892, 11/4/04) or KATRE (US Patent 4,931,544) or KILBANOV (US Patent 4,414,147) or HOLCENBERG (J.S. Holcenberg, et al. J. Biol. Chem. (1975) 250(11), pages 4165-4170) or HALL (US Patent 4,144,333) or GUTHEIL (US Patent 5,574,107) or LaROCHELLE (US Patent 5,833,986).

The instant claims are drawn generally to compositions of the formula:

[negatively charged protecting group]-$(aa)_n$X-$(aa)_4$-[therapeutic agent], where X is a non-genetically encoded amino acid, n is 0-15 and each aa is any amino acid. The compound must be cleavable by TOP.

Trouet teaches βAla-Leu-Ala-Leu-(Dox/Dnr) (table 1, page 25). Trouet teaches the compounds as pharmaceutical compositions (e.g. Figures 20 and 21).

Li teaches succinylation of ACTH, and that succinylation reduced the number of trypsin cleavage products (e.g. Figure 3, page 2639) and further teaches that glucagon, prolactin, lysozyme and ribonuclease have been succinylated and that the products, "are completely soluble in aqueous solution of a pH above 5" (page 2640).

DeJongh teaches succinylation of peptides for mass spectrometry (throughout).

Katre teaches succinylated IL-2 (e.g. Examples I and II). Katre teaches that succinylation increases aqueous solubility, "under ambient conditions at pharmaceutically acceptable pH ranges," and that, "succinylation also avoids addition of extraneous solubilizing additives [...] to keep the protein in solution. [...] The *in vivo* half life may be modulated by selecting appropriate conditions such as degree of succinylation." (column 2, lines 17-28). Katre provides that others have studied the properties, "of various succinylated proteins" (column 1, line 65 to column 2, line 3).

Kilbanov teaches interferon reacted with dicarboxylic anhydrides such as succinic, maleic, copoly(ethylene maleic) aka PEMA (e.g. column 5, lines 24-46). Succinylation of interferon decreases hydrophobicity.

Holcenberg (cited by Katre) teaches succinylation of glutaminase-asparaginase and that, "These modifications markedly prolonged the half-lives of the enzyme in mice, rats, and rabbits. [...] Succinylation protected the enzyme from trypsin digestion." (*Summary*, page 4165).

The difference between Trouet and the instant claims, is that while Trouet teaches the core βAla-Leu-Ala-Leu-(Dox/Dnr), Trouet does not teach succinylated βAla-Leu-Ala-Leu-(Dox/Dnr).

Gutheil and Hall are provided for the beneficial teachings that succinyl and other dicarboxylic acid moieties are well known in the art as amino acid protecting groups (Gutheil-column 9; Hall, column 3). Gutheil teaches that the protecting group, "protect the reactive functional group from undesirable chemical reactions."

LaRochelle is provided for the beneficial teachings that pharmaceutical compositions formulation is routine in the art (e.g. column 10, lines 39-59, citing *Remington's*).

Applicant's arguments presented May 4, 2005 have been reconsidered. Applicant argued that the compounds have, "unexpected reduced toxicity *in vivo* compared to the compounds without neutral or negatively charged stabilizing groups" (page 14, *Remarks* of 5/4/05). Further, Applicant argues that the references would not have been combined because the compounds of Trouet are not peptide hormones.

In response to applicant's argument that it would not have been expected to discover the reduced toxicity and that there was no motivation to study the peptides by mass spectrometry, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Further, Applicant states in the specification that (Suc/Gl)-βAla-Leu-Ala-Leu-Dox dosed mice survived up to 8 days when treated with 250 mg/kg bolus. Additionally, while Applicant states that the succinylated form was significantly less toxic than the βAla-Leu-Ala-Leu-Dox form, Applicant's specification states, "These data support the hypothesis that the acute toxicity is due to a positively charged aggregate causing a similar effect to that seen for protamines or polylysine." (page 65). The hypothesis is that the negative charge reduces toxicity because it

reduces aggregation. Applicant's arguments (5/4/05) did not address the *prima facie* case set forth by the examiner (11/4/04) to the extent that the toxicity reduction could have been due to an increase in half-life of the compound, nor did Applicant provide sufficient evidence that the whole genus would have this 'unexpected result', based on one compound having reduced toxicity. Applicant asserts that the toxicity is greatly reduced for Suc-βAla-Leu-Ala-Leu-Dox, however the instant specification and/or the teachings of Trouet do not present a toxicity study for the compound βAla-Leu-Ala-Leu-Dox, and thus no comparison can be made and therefore the examiner improperly agreed that the evidence of 'unexpected results' was convincing.

Additionally, it is noted that Applicant had, themselves, studied the instant compounds by mass spectrometry (Example 12, page 51), and thus would have derived the same benefit relied upon by the examiner in previous rejection using DeJongh.

It would have been obvious at the time of the invention to have succinylated βAla-Leu-Ala-Leu-(Dox/Dnr) in order to protect it from 'undesirable reactions' such as trypsin digestion *in vivo* or to decrease hydrophobicity and to increase the half-life and to formulate it in a pharmaceutical with a carrier.

It is noted that the compounds βAla-Leu-Ala-Leu-(Dox/Dnr) are hydrophobic peptide conjugates.

One would have been motivated to have succinylated βAla-Leu-Ala-Leu-(Dox/Dnr) in order to reduce the undesirable trypsin digestion *in vivo*, to decrease the hydrophobicity and increase the solubility and to increase the half-life, as taught by the references above.

One would have had a reasonable expectation for success in succinylating βAla-Leu-Ala-Leu-(Dox/Dnr) and thereby reducing the undesirable trypsin digestion *in vivo*, decreasing the

hydrophobicity and increasing the solubility and increasing the half-life, as succinylation is a routinely practiced technique in the peptide arts.

One would have been motivated to make the succinylated composition into a pharmaceutical in order to compare the succinylated product to the free form and determine to what extent the *in vivo* half-life, trypsin digestion and solubility had been modified.

One would have had a reasonable expectation for success in making the compound into a pharmaceutical composition, as pharmaceutical compositions are routinely prepared in the medicinal arts, and because Trouet teaches the core βAla-Leu-Ala-Leu-(Dox/Dnr) in pharmaceuticals.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, 120 and 122-124 are rejected under 35 U.S.C. 103(a) as being obvious over TROUET (US Patent 5,962,216; F13: PTO-1449 of 11/30/01) in view of LI (PTO-892, 11/4/04) or KATRE (US Patent 4,931,544) or KILBANOV (US Patent 4,414,147) or HOLCENBERG (J.S. Holcenberg, et al. J. Biol. Chem. (1975) 250(11), pages 4165-4170) or HALL (US Patent 4,144,333) or GUTHEIL (US Patent 5,574,107) or LaROCHELLE (US Patent 5,833,986).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by:

> (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another";
> (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131;
> (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c); or
> (4) showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). *See MPEP § 706.02(l)(1) and § 706.02(l)(2).*

The instant claims are presented *supra*. The teachings of Li, DeJongh, Katre, Kilbanov, Holcenberg, Gutheil and LaRochelle are presented *supra*.

Trouet teaches βAla-Leu-Ala-Leu-(Dox/Dnr) (e.g. claims 3; SEQ ID NOs:1, 2; Table 1, column 13). Trouet teaches the compounds as pharmaceutical compositions (e.g. Figures 20 and 21; column 18, lines 17-20).

One would have been motivated to have succinylated βAla-Leu-Ala-Leu-(Dox/Dnr) in order to reduce the undesirable trypsin digestion *in vivo*, to decrease the hydrophobicity and increase the solubility and to increase the half-life, as taught by the references above.

One would have had a reasonable expectation for success in succinylating βAla-Leu-Ala-Leu-(Dox/Dnr) and thereby reducing the undesirable trypsin digestion *in vivo*, decreasing the hydrophobicity and increasing the solubility and increasing the half-life, as succinylation is a routinely practiced technique in the peptide arts.

One would have been motivated to make the succinylated composition into a pharmaceutical in order to compare the succinylated product to the free form and determine to what extent the *in vivo* half-life, trypsin digestion and solubility had been modified.

One would have had a reasonable expectation for success in making the compound into a pharmaceutical composition, as pharmaceutical compositions are routinely prepared in the medicinal arts, and because Trouet teaches the core βAla-Leu-Ala-Leu-(Dox/Dnr) in pharmaceuticals.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, 120 and 122-124 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims

1-19, 25-37 and 40-42 of TROUET(U.S. Patent No. 5,962,216) in view of Li, DeJongh, Katre, Kilbanov, Holcenberg, Gutheil and LaRochelle.

The teachings of Trouet, Li, DeJongh, Katre, Kilbanov, Holcenberg, Gutheil and LaRochelle are presented *supra*.

Trouet teaches βAla-Leu-Ala-Leu-Dox (claims 3). Trouet teaches the compounds as pharmaceutical compositions (claims 19 and 37).

MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (*emphasis added*). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)."

In looking to the specification for definitions and support for the products claimed beyond βAla-Leu-Ala-Leu-Dox, the specifically contemplated embodiments which provide support for the claims are found within the examples and tables, e.g. Table 1 and Examples 1-14, which include the Dnr conjugate.

One would have been motivated to have succinylated βAla-Leu-Ala-Leu-(Dox/Dnr) in order to reduce the undesirable trypsin digestion *in vivo*, to decrease the hydrophobicity and increase the solubility and to increase the half-life, as taught by the references above.

One would have had a reasonable expectation for success in succinylating βAla-Leu-Ala-Leu-(Dox/Dnr) and thereby reducing the undesirable trypsin digestion *in vivo*, decreasing the hydrophobicity and increasing the solubility and increasing the half-life, as succinylation is a routinely practiced technique in the peptide arts.

One would have been motivated to make the succinylated composition into a pharmaceutical in order to compare the succinylated product to the free form and determine to what extent the *in vivo* half-life, trypsin digestion and solubility had been modified.

One would have had a reasonable expectation for success in making the compound into a pharmaceutical composition, as pharmaceutical compositions are routinely prepared in the medicinal arts, and because Trouet teaches the core βAla-Leu-Ala-Leu-(Dox/Dnr) in pharmaceuticals.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 2, 3, 5-12, 14, 15, 17-19, 21, 23-27, 30, 37 and 122-124 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-8, 11, 13-18, 23-29, 57, 58, 60, 61 and 63 of copending Application No. 10/311,411 (PICKFORD). This rejection is set forth in view of the amendments filed January 6, 2006 in Pickford.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are of an overlapping scope, both being generally drawn to stabilizer-peptide-therapeutic conjugates and pharmaceutical compositions, thereof.

Furthermore, the compounds claimed by Pickford are species of the instant claims, e.g. claim 23 of Pickford. Further, the compounds of Pickford need only be cleavable by another

enzyme, but does not require that the compounds are not cleavable by TOP, and thus the compounds of Pickford either anticipate, or are anticipated by, the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Ownership / Inventorship

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118, 119, 120 and 122-124 are directed to an invention not patentably distinct from claims 1-19, 25-37 and 40-42 of TROUET(U.S. Patent No. 5,962,216), for the reasons set forth *supra* under Double Patenting.

Claims 2, 3, 5-12, 14, 15, 17-19, 21, 23-27, 30, 37 and 122-124 are directed to an invention not patentably distinct from claims 1, 4-8, 11, 13-18, 23-29, 57, 58, 60, 61 and 63 of PICKFORD (copending Application No. 10/311,411), for the reasons set forth *supra* under Double Patenting.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned Trouet and/or Pickford, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made.

In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly

assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

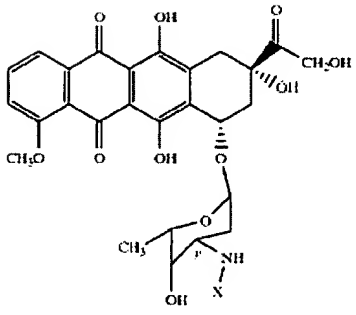
> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In the interest of compact prosecution, the search has been extended as set forth below.

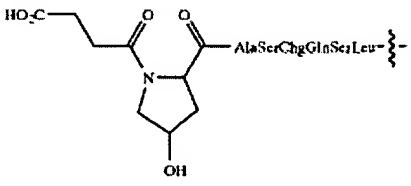
Claims 2, 3, 5-8, 11, 14-16, 18, 19, 23-26, 30, 37 and 122-123 are rejected under 35 U.S.C. 102(e) as being anticipated by GARSKY (US Patent 5,948,750).

The instant claims are presented *supra.*

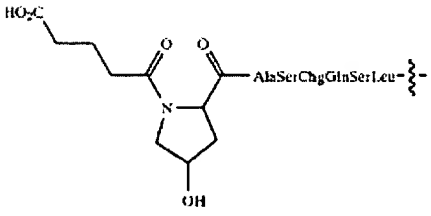
Garsky teaches conjugates of the following formulae:



, where X is:



(SEQ ID NO: 69) or



(SEQ ID NO: 71), or any of SEQ ID NOs: 75-82, 84, 87 or 88 (e.g. claim 14) and pharmaceuticals of said compounds (claim 25).

In the instant case, as exemplified by SEQ ID NO:69, the compound is [dicarboxylic acid]-$(aa)_3$-X-aa_3-Dox, specifically, Suc-Hyp-Ala-Ser-Chg-Gln-Ser-Leu-Dox. Chg is a 'non-genetically encoded amino acid'. Because the structural limitations of the compound are satisfied, the compound necessarily possesses the properties that are claimed, e.g. that of reduced toxicity *in vivo*, cleavage by TOP, etc., as a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Conclusion

NO CLAIMS ARE ALLOWED.

The prior art made of record on the attached PTO-892 and not relied upon in any rejection is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Andrew D. Kosar, Ph.D.
Art Unit 1654

ANISH GUPTA
PRIMARY EXAMINER

Notice to Comply	Application No. 09879442	Applicant(s) DUBOIS ET AL.	
	Examiner **Andrew D. Kosar**	Art Unit 1654	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Sequences are found in the specification that are not listed in the sequence listing

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY